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I, JULIE BILLINGSLEY, TEAM LEADER EXAMINATION SUPPORT AND SALES hereby certify that annexed is a true copy of the Provisional specification in connection with Application No. PR 7380 for a patent by AUSTRALIAN BIOMEDICAL COMPANY PTY LTD as filed on 31 August 2001.

WITNESS my hand this
Second day of February 2004

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AUSTRALIA
Patents Act 1990

P/00/009
Regulation 3.2

Provisional Specification

Invention Title

COMPOUNDS FOR MEDICINAL PURPOSES

The invention is described in the following statement

3 pages Documents attatched

Compounds For Medicinal Purposes

Abstract:

This invention provides a novel application of Gibberellins and their derivatives for the preparation of a pharmaceutical composition or medicaments for the treatment of diabetes and related conditions.

Field of the invention:

The present invention relates to the application of a group of compounds known as Gibberellins and their derivatives (described in PCT/AU/96/00003) for the preparation of a pharmaceutical composition for the treatment of diabetes and related conditions, as well as a method for treating these and other conditions by administering Gibberellin on a pharmaceutically acceptable salt or esters including glycoside esters, active esters or lactones. Moreover, this invention relates to the manufacturing and the use of a medicament for treating diabetes and related conditions thereof. Furthermore, the application of Gibberellins and their derivatives especially by oral, transdermal patches, or by inhalation administration can be used as a substitute for insulin and/or IGF (Insulin like Growth Factor) treatment or as a choice of combination therapy with insulin, IGF, growth factors or other pharmaceutically compatible anti-diabetic agents for the treatment of diabetes and related conditions.

Disclosure of the invention:

We have found that Gibberellins and their derivatives are angonists of growth factors such as EGF (Epidermal Growth Factor), IGF-1, IGF-2 (Insulin like Growth Factor), TGF-β, FGF-1, FGF-2, PDGF and so on.

The experimental results suggested that Gibberellins, which are generated by plants and microbes, act as broad spectrum binders binding to a range of growth factor receptors. They differ from the growth factors found in animals, each of which has a high affinity for a specific receptor. This is the result of evolution. The biological systems of plants and microbes produce biological substances acting on a broader (less specific) base than that of the more complex life forms such as animals.

Since Gibberellins are smaller molecules than growth factors, the binding of Gibberellins on the growth factor receptors is probably weaker, but Gibberellins may overcome that by binding to more receptor sites. In the absence of growth factors, Gibberellins bind to growth factor receptors to stimulate cell growth and other functions as individual growth factor presents. Under this condition, Gibberellins perform the functions of the growth factors. In the presence of growth factors, the growth factors bind to their receptors more readily due to their higher affinity for those receptor sites. The physical bulkiness of these growth factors leave no room or very little room at the receptor sites for which Gibberellins can bind. This results in Gibberellins being ineffective when growth factors are present in sufficient quantities. This mechanism provides a very good profile for Gibberellins acting as a substitute for growth factors including IGF since the presence of excess Gibberellins will not interfere with the normal functions of these growth factors.

It is known that insulin, IGF and EGF receptors are all in the same family and their structures are expected to be have 90% similarity. Therefore, it may be logically expected that Gibberellins could play a role not only as a substitute for growth factors but also as a substitute for insulin.

Diabetes mellitus is a chronic disorder manifested by hyperglycemia and altered lipid and protein metabolism. According to the American Diabetes Association, more than 13 million people in the U.S. suffer from diabetes, and each year some 650,000 new cases are identified. The introduction of insulin and of sulfonyl ureas represented important landmarks in the treatment of diabetes mellitus. Insulin like growth factor – 1 (IGF-1), a molecule with structure homology to insulin, has its own specific receptor, the type-1 IGF receptor, through which it elicits a variety of metabolic effects that are similar to insulin. The discovery of the active region of human growth factor responsible for the insulin like actions of the molecule has led to the development of its fragment as new anti-diabetic peptide agent. It is also known that growth factors are polypeptides that regulate the replication, differentiation and metabolic homeostasis cells. They increase

the growth and/or survival of neurons. IGF-2 is known to increase the rate of nerve regeneration, in pre-clinical testing for the treatment of various neurological disorders including diabetic neuropathies. Furthermore, elevated intracellular concentrations of c-AMP potentiate glucose-dependent insulin secretion from pancreatic β-cells. It is known that Gibberellins increase the activity of adenylate and gryanylate cyclase. The intracellular concentrations of c-AMP and c-GMP may therefore be increased by the administration of Gibberellins as the consequence to potentiate glucose-dependent insulin secretions from pancreatic β-cells. From the review described above, it may be logically expected to apply Gibberellins for the treatment of diabetes. Thus this invention provides an aspect use of Gibberellins and their derivatives for the treatment of diabetes and related conditions. Furthermore, this invention would be extended as described in the "Field of the invention".

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